



Toxicogenomics: Principles and Applications

Edited by Hisham K. Hamadeh and Cynthia A. Afshari

Hoboken, NJ: Wiley-Liss, 2004. 361 pp. ISBN: 0-471-43417-5. \$69.95 cloth

This timely book presents basic toxicology for molecular biologists and detailed approaches and methods of gene expression, protein, and metabolic global analyses for toxicologists and others learning to use such methods. There are high expectations that “molecular signatures” will become useful as biomarkers of exposure, early effect, and differential susceptibility

and reveal targets for new drugs. I particularly appreciated the effort to link genotypes to phenotypes in the form of “target organ toxicity patterns”—in liver, kidney, lung, nervous system, skin, reproductive system—from Chapter 1 onward. The detailed pathology and physiology along the periportal–centrilobular gradient in liver, combined with references to mRNA analyses of 15 hepatotoxins, and along the segments of the renal tubule exposed to cisplatin or ochratoxins, illustrate (e.g., Chapter 8) the opportunity to link traditional toxicology and pathology with the molecular analyses. Conversely, global molecular analyses have begun to reveal many previously unsuspected or unknown targets for desired and adverse effects of drugs and other chemicals.

The aim of the new approaches is to transform toxicology from descriptive to predictive, including prediction of *in vivo* effects from *in vitro* models and other species. Technical features are presented in considerable detail. Innovative manufacture, miniaturization, scanning, and statistical analyses of DNA microarrays have yielded sequence and gene expression information with remarkable throughput. Many technical advances are still needed, such as better evidence that fluorophores match up well in two-color experiments. Statistical analyses of a methapyriline study vividly demonstrate sources of “false discoveries” (Chapter 6). Differential cell loss in heterogeneous tissues will change mRNA ratios, requiring estimates by pathologists of changes in tissue composition. Expressed sequence tags unannotated for function may be

discriminants for disease associations (Chapter 9). *In vitro* response patterns may not match *in vivo* patterns (Chapter 10). When pathways and regulation are highly conserved, yeast cells or other model organisms may reveal a lot about the multiple targets and interactions of a drug or its intended protein target.

“Toxicogenomics” is defined explicitly to embrace proteins and metabolites as the key effector classes in functional genomics. There are two chapters on proteomics and one on metabolomics and metabolomics. Multiple, rapidly evolving fractionation, chemical tagging, mass spectrometry, microarray format affinity methods, and database search algorithms are highlighted; key challenges are much higher throughput, validation of protein identifications, and quantitation. Plasma and tissue lysate proteomes are very complex mixtures, reflecting the huge range of concentrations and many isoforms of large numbers of proteins, and the dynamic nature of the structure–function relationships. International cooperative strategies are recommended (Chapter 12). Proteins are targets of many environmental agents, with potential effects on all functions and pathways in the cell, including the posttranslational modification of proteins themselves. Peptide adducts with electrophiles have been characterized and mapped on target proteins with tandem mass spectrometry scans and SALSA software (Chapter 13); finding low abundance targets and focusing instrument time on peptides of highest interest are big challenges. Finally, metabolic profiles of toxicologic exposures have yielded many potential markers of early effects.

The editors, formerly at the National Institute of Environmental Health Sciences (NIEHS) Center for Toxicogenomics and now at Amgen Inc., and their colleagues from the NIEHS, academe, and many companies have highlighted emerging techniques, practical laboratory planning, and explicit biostatistical and bioinformatic interpretations. The book is well referenced, with particular attention to web-based resources. The emphasis on methods rather than signatures reveals the still-early nature of this promising field.

GILBERT S. OMENN

Gilbert S. Omenn is professor of internal medicine, human genetics, and public health at the University of Michigan. His research interests include cancer proteomics, chemoprevention of cancers, public health genetics, science-based risk analysis, and health policy. He leads the Plasma Proteome Project for the international Human Proteome Organization and is president-elect of the American Association for the Advancement of Science.

Announcements | New Books

Algorithms in Bioinformatics

Inge Jonassen, Junbyong Kim, eds.
New York: Springer-Verlag, 2004. 476 pp.
ISBN: 3-540-23018-1, \$84

Antisense Therapeutics, 2nd ed.

M. Ian Phillips
Totowa, NJ: Humana Press, 2004. 344 pp.
ISBN: 1-58829-205-3, \$125

Assembling the Tree of Life

Joel Cracraft, Michael J. Donoghue
New York: Oxford University Press, 2004.
592 pp. ISBN: 0-19-517234-5, \$59.95

Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins, 3rd ed.

Andreas D. Baxevasis, B.F. Francis Ouellette, Mark Boguski, Gerard Bouffard, Stephen Bryant, Barbara Butler, Sam Cartinhour, Colombe Chappey, Mark Hershkovitz, Christopher Hogue, Jonathan Kams, David Landsman, Detlef Leipe, James Ostell, Greg Schuler
Hoboken, NJ: John Wiley & Sons, 2004. 512 pp.
ISBN: 0-471-47878-4, \$79.95

Cancer Gene Therapy

David T. Curiel, Joanne T. Douglas
Totowa, NJ: Humana Press, 2004. 504 pp.
ISBN: 1-58829-213-4, \$165

Epigenetics Protocols

Trygve O. Tollefsbol
Totowa, NJ: Humana Press, 2004. 320 pp.
ISBN: 1-58829-336-x, \$99.50

Gene Genealogies, Variation and Evolution: A Primer in Coalescent Theory

Jotun Hein, Mikkel Schierup, Carsten Wiuf
New York: Oxford University Press, 2004.
350 pp. ISBN: 0-19-852995-3, \$124.50

Genome Transcriptome and Proteome Analysis

Alain Bernot
Hoboken, NJ: John Wiley & Sons, 2004. 240 pp.
ISBN: 0-470-84954-1, \$115

Guide to Mutation Detection

Graham R. Taylor, Ian N. Day
Hoboken, NJ: John Wiley & Sons, 2004. 352 pp.
ISBN: 0-471-23444-3, \$89.95

Mobile Genetic Elements: Protocols and Genomic Applications

Wolfgang J. Miller, Pierre Capy
Totowa, NJ: Humana Press, 2004. 304 pp.
ISBN: 1-58829-007-7, \$89.50

Modular Protein Domains

Giovanni Cesareni, Marlo Gimona, Martus Sudol, Michael Yaffe, eds.
Totowa, NJ: Humana Press, 2004. 524 pp.
ISBN: 3-527-30813-X, \$185

Oligonucleotide Synthesis

Piet Herdewijn
Totowa, NJ: Humana Press, 2004. 456 pp.
ISBN: 1-58829-233-9, \$125

Protein Synthesis and Ribosome Structure: Translating the Genome

Knud H. Nierhaus, Daniel N. Wilson
Hoboken, NJ: John Wiley & Sons, 2004. 592 pp.
ISBN: 3-527-30638-2, \$180

Statistical Methods in Molecular Evolution

Rasmus Nielsen, ed.
New York: Springer-Verlag, 2004. 520 pp.
ISBN: 0-387-22333-9, \$89.95

Stroke Genomics: Methods and Reviews

Simon J. Read, David Virley
Totowa, NJ: Humana Press, 2004. 352 pp.
ISBN: 1-58829-333-5, \$125

Thompson & Thompson Genetics in Medicine, Revised

Robert Nussbaum, Roderick McInnes, Huntington Willard
New York: Springer-Verlag, 2004. 540 pp.
ISBN: 0-7216-0244-4, \$49.95

The Proteus Effect: Stem Cells and Their Promise

Ann B. Parson
Washington, DC: National Academies Press, 2004.
256 pp. ISBN: 0-309-08988-3, \$24.95

Transcription Factors

Manfred Gossen, Jörg Kaufmann, Steven J. Triezenberg, eds.
New York: Springer-Verlag, 2004. 581 pp.
ISBN: 3-540-21095-4, \$399

Understanding DNA: The Molecule and How it Works

Chris Calladine, Honore Drew, Ben Luisi, Andrew Travers
New York: Springer-Verlag, 2004. 352 pp.
ISBN: 0-12-155089-3, \$45

Welcome to the Genome: A User's Guide to the Genetic Past, Present, and Future

Rob DeSalle
Hoboken, NJ: John Wiley & Sons, 2004. 240 pp.
ISBN: 0-471-45331-5, \$29.95